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mesothelioma

155O CHEMOTHERAPY OF MALIGNANT PLEURAL MESOTHELIOMA DOES NOT PRECLUDE USE OF CHECK-POINT BLOCKADE

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Background: Mesothelioma is an aggressive cancer with short survival and urgent need of new therapeutic options. Based on preclinical data, immunotherapy may be a promising approach to treat this disease. However, it is not known whether chemotherapy influences the expression of molecules targeted by check-point blockade such as Programmed Death Receptor 1 (PD-1), its ligands, PD-L1 (B7-H1) and PD-L2 (B7-DC), CD275 (ICOS-L) and CD276 (B7-H3).

Methods: We therefore analyzed the expression of HLA-I, II, PD-L1, ICOS-L and B7-H3 in 88 tumor samples derived from untreated mesothelioma patients using a Tissue Microrarray (TMA). In addition, we evaluated the expression of these molecules on matching whole tumor sections from 10 patients before and after chemotherapy. Finally, we analyzed the expression of HLA-I, II, PD-L1, ICOS-L and B7-H3 on mesothelioma cell lines, upon treatment with cisplatin/pemetrexed or gemcitabine.

Results: We found that tumor cells expressed HLA-I in 79/88 samples (90%); HLA-II in 14/88 samples (16%), PD-L1 in 14/88 samples (16%), ICOS-L in 45/88 samples (50%) and B7-H3 in 55/80 samples (69%) on TMA. We observed no down-regulation of any of the investigated molecules on matching whole tumor sections from patients before and after treatment with cisplatin/pemetrexed. This result was also confirmed using mesothelioma cell lines.

Conclusions: Our results demonstrate that chemotherapy of mesothelioma does not preclude use of check-point blockade.

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